psychological maturity and thus with different and often conflicting values. And perhaps most basic of all will be the question of individual rights. It will be necessary, but difficult, somehow to achieve the necessary discipline in human behavior, whether this be in procreation or whatever, in the common interest of humanity without unduly infringing upon the rights of individual well-being and self-fulfillment for which the human race has been fighting so hard for so long.

For many years there have been pioneering efforts to draw attention to ecological problems and to do something about them. The pioneers are to be found among the family planners and the conservationists. Progress has been slow and opposition from powerful moral and economic interests has been strong. Now quite suddenly ecology is "in." The present danger is that this may prove to be a mere flash in the pan when what is needed is the sustained heat and energy of a controlled nuclear reaction. This is a task not just for the 1970s but for the whole rest of the life span of humanity.

Carotid Sinus Stimulation For the Treatment Of Angina Pectoris

DURING THE PAST DECADE several important new therapeutic approaches for the treatment of the clinical syndrome of angina pectoris have been developed. It is now generally accepted that the basic cause of angina pectoris is inadequate delivery of oxygen to the myocardium for its demands or needs to perform a specific task. Recently, however, the new approaches to therapy for this clinical condition have resulted from important physiological observations on control of coronary blood flow and a better understanding of hemodynamic and biochemical factors relating to the initiation of the anginal syndrome. Some of these are a clear demonstration that a rise in arterial blood pressure frequently precedes an attack of spontaneous angina pectoris, that factors which enhance sympathetic nervous stimulation to the heart increase myocardial oxygen consumption by increasing heart rate and the rate at which the left ventricle develops tension,[1] that anaerobic metabolism and lactate production occur during myocardial ischemia, and that the parasympathetic nervous system may play a role in controlling coronary vascular resistance.[2] Utilizing these physiologic concepts, several new modes of therapy have been proposed for treating patients with incapacitating angina pectoris. Propranolol was introduced for treating patients with angina pectoris with the concept that blocking excessive sympathetic stimulation to the heart would allow an individual to perform more work with less demand for increased myocardial oxygen delivery.[3,4] Furthermore, combination therapy with nitrites and propranolol has been advocated to lower blood pressure acutely and to inhibit sympathetic stimulation of the myocardium.

More recently, Braunwald and his colleagues have introduced the concept of carotid sinus stimulation for relieving angina pectoris and allowing patients to perform more exercise without developing angina, or for treatment of established anginal attacks.[5,6] The Specialty Conference appearing elsewhere in this issue presents the physiological basis on which this treatment was introduced and a report of preliminary experience with its use in patients with incapacitating angina pectoris. For many years it has been known that the circulatory response to carotid sinus stimulation included reductions in heart rate, in arterial pressure and in systemic vascular resistance. All of these responses would be expected to reduce angina pectoris, and it was on these principles that Lown and Levine in 1951 proposed a diagnostic test for the relief of angina pectoris by carotid sinus stimulation.[7] A number of physiological studies utilizing the carotid sinus stimulator have clarified the circulatory response to repeated carotid sinus stimulation in awake unanesthetized man.[8] The decrease in arterial pressure, which is far greater than the decrease in heart rate and in cardiac output, appears to be the major factor in preventing the occurrence of angina pectoris and in relieving already established attacks. The observation that patients who use the carotid sinus stimulator for several months

then have less angina and greater exercise tolerance even when not activating their stimulator is interesting and as yet unexplained. Perhaps this reflects the clinical course of coronary artery disease and its unpredictable nature. Braunwald and colleagues clearly recognize the difficulties in assessing treatment for angina pectoris, but they have convincingly demonstrated a significant effect of carotid sinus stimulation in their small, selected group of patients.

The clinical results presented are preliminary, and the authors stress that long-term follow-ups are not available, that the implantation of the stimulation electrodes requires an operation not without risk, that carotid sinus stimulation itself has inherent dangers (death may occur from it), and finally that careful patient selection for the procedure is essential. They also point out that carotid sinus stimulators may be useful in the management of patients with paroxysmal atrial arrhythmias unresponsive to drug therapy.

Although the report in this issue of the journal suggests that the major benefit of carotid sinus stimulation is due to a reduction in arterial pressure, a recent report[2] showed that parasympathetic stimulation to the heart by vagal nerve stimulation (which is equivalent to carotid sinus stimulation in animals) reduced coronary vascular resistance and increased coronary flow. Perhaps this is an additional mechanism by which carotid sinus stimulation improves angina pectoris. These studies must be confirmed and expanded and may lead to other new approaches to the treatment of patients with intractable angina.

From the evidence available, it appears that the technique of carotid sinus stimulation merits further study and more widespread application for the treatment of carefully selected patients with angina pectoris who are resistant to other modes of therapy. Long-term follow-up studies and studies in a group of age-matched and disease-matched control patients will be needed before this unique method of treatment can be placed in perspective.

DONALD C. HARRISON, M.D.
Cardiology Division
Stanford University School of Medicine

REFERENCES

1. Braunwald E: 13th Bowditch Lecture. The determinants of myocardial oxygen consumption. The Physiologist 12:69-93, 1969

2. Feigl EO: Parasympathetic control of coronary blood flow in dogs. Circ Res 25:509-519, 1969

3. Hamer J, Grandjean T, Melendez L, et al: Effect of propranolol (Inderal®) in angina pectoris. A preliminary report. Brit Med J 2: 720-721, 1964

4. Gilliam PMS, Prichard BNC: Use of propranolol in angina pectoris. Brit Med J 2:337-339, 1965

5. Braunwald E, Epstein SE, Glick G, et al: Relief of angina pectoris by electrical stimulation of the carotid-sinus nerves. New Eng J Med 277:1278-1283, 1967

6. Epstein SE, Beiser GD, Goldstein RE, et al: Treatment of angina pectoris by electrical stimulation of the carotid-sinus nerves. New Eng J Med 280:971-977, 1969

7. Lown B, Levine SA: Carotid sinus: Clinical value of its stimulation. Circulation 23:766-789, 1961

8. Epstein SE, Beiser GD, Goldstein RE, et al: Circulatory effects of electrical stimulation of the carotid-sinus nerves in man. Circulation 40:269-275, 1969

Hemostatic Mechanisms In Thrombogenesis: Implications for Therapy

ELSEWHERE IN THIS JOURNAL Dr. Daniel Deykin has summarized important advances in our understanding of the physiologic mechanisms of hemostasis. He has related these mechanisms to the pathogenesis of the three types of thrombosis seen in patients: the small white thrombus that may occlude a diseased artery; the large red thrombus that may form in a vein or a chamber of the heart; and the fine fibrin thrombi that may be found in the microcirculation after diffuse clotting in the flowing blood. Of practical importance, Dr. Deykin has pointed out how the different role of the blood clotting reactions in these disorders can explain the different effectiveness of anticoagulant therapy in each. Since thrombosis may occur in any patient, physicians in all branches of medicine should profit from a careful reading of his Medical Progress article.

The hemostatic process may be divided into two overlapping steps. In the first, platelets accumulate at the site of vessel wall injury. When the endothelial lining of the vessel is broken, platelets adhere to collagen in exposed connective tissues; interact with the collagen and release ADP; and, as a result of an action of this released ADP, stick to each other to form aggregates. These early aggre-